

CORRECTED VERSION

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
1 February 2001 (01.02.2001)

PCT

(10) International Publication Number  
WO 01/07107 A3

(51) International Patent Classification<sup>7</sup>: A61M 15/00, A61J 3/07

(21) International Application Number: PCT/US00/40454

(22) International Filing Date: 21 July 2000 (21.07.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/145,464 23 July 1999 (23.07.1999) US  
60/206,123 22 May 2000 (22.05.2000) US

(71) Applicant: PHARMACEUTICAL DISCOVERY CORPORATION [US/US]; 33 West Main Street, 4th Floor, Elmsford, NY 10523 (US).

(72) Inventors: STEINER, Solomon, S.; 24 Old Wagon Road, Mount Kisco, NY 10507 (US). POOLE, Trent; 59 Country Corners Road, South Amherst, MA 01002 (US). FELDSTEIN, Robert; 1155 Warburton Avenue, Yonkers, NY 10701 (US). FOG, Per, B.; 199 Green Lane, Bedford Hills, NY 10507 (US).

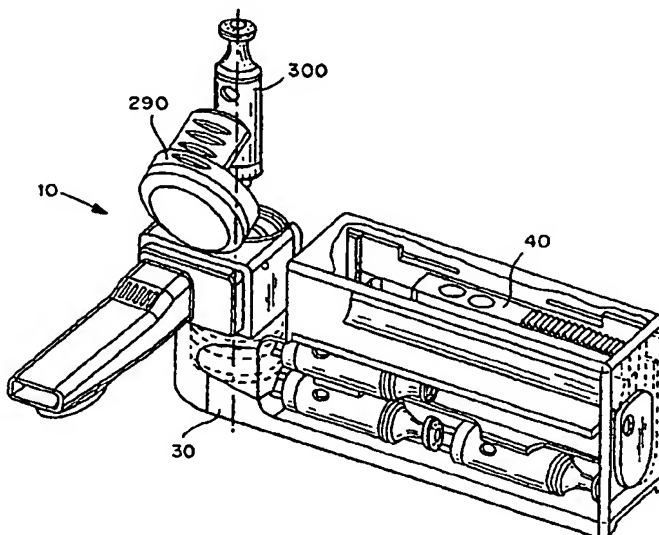
(74) Agents: PABST, Patrea, L. et al.; Arnall Golden & Gregory, LLP, 2800 One Atlantic Center, 1201 West Peachtree Street, Atlanta, GA 30309-3450 (US).

(81) Designated States (*national*): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian

[Continued on next page]

(54) Title: UNIT DOSE CAPSULES AND DRY POWDER INHALER



(57) Abstract: The dry powder inhaler (10) comprises an intake section (20); a mixing section (30), and a mouthpiece (40). The mouthpiece is connected by a swivel joint to the mixing section, and may swivel back into the intake section and be enclosed by a cover (290). The intake chamber comprises a piston with a tapered piston rod and spring, and one or more bleed-through orifices to modulate the flow of air through the device. It optionally comprises a feedback module to generate a tone indicating when the proper rate of airflow has been achieved. The mixing section holds a capsule (300) with holes containing a dry powder medicament, and further opens and closes the capsule when the intake section is at a certain angle to the mouthpiece. The mixing section is a Venturi chamber to impart a cyclonic flow to air passing through the mixing chamber.

WO 01/07107 A3



patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(48) Date of publication of this corrected version:

12 July 2001

(15) Information about Correction:

see PCT Gazette No. 28/2001 of 12 July 2001, Section II

Published:

.. With international search report.

(88) Date of publication of the international search report:

21 June 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

## **UNIT DOSE CAPSULES AND DRY POWDER INHALER**

### **FIELD OF THE INVENTION**

The present invention is in the field of inhalers.

### **BACKGROUND OF THE INVENTION**

In the early 1970's it was found that certain medicines could be administered in dry-powder form directly to the lungs by inhalation through the mouth or inspiration through the nose. This process allows the medicine to bypass the digestive system, and may, in certain cases, allow smaller doses to be used to achieve the same results or orally ingested or injected medicines. In some cases, it provides a delivery technique that reduces side effects for medicines taken by other medicines.

Inhaler devices typically deliver their medicinal in a liquid mist or a powder mist. The liquid mist is typically created by a chlorofluorocarbon propellant. However, with the ban on chlorofluorocarbons by the Montreal protocol, interest has turned to dry powder inhalers.

For a dry powder inhaler to work effectively, it must deliver fine particles of medicinal powder that do not agglomerate, and do not end up striking, and being absorbed by the patient's mouth or upper oropharyngeal region. Air flow must therefore not be too fast. Furthermore, it should not be difficult for a patient to load with medicine or to use with the proper technique. Current dry particle inhalers fail in one or more of these important criteria.

### **SUMMARY OF THE INVENTION**

Described is a dry powder inhaler comprising an intake section; a mixing section, and a mouthpiece. The mouthpiece is connected by a swivel joint to the mixing section, and may swivel back onto the intake section and be enclosed by a cover. The intake chamber comprises a special piston with a tapered piston rod and spring, and one or more bleed-through orifices to modulate the flow of air through the device. The intake chamber further optionally comprises a feedback module to generate a tone indicating

to the user when the proper rate of airflow has been achieved. The mixing section holds a capsule with holes containing a dry powder medicament, and the cover only can open when the mouthpiece is at a certain angle to the intake section. The mixing section further opens and closes the capsule when the intake section is at a certain angle to the mouthpiece. The mixing section is a Venturi chamber configured by protrusions or spirals to impart a cyclonic flow to air passing through the mixing chamber. The mouthpiece includes a tongue depressor, and a protrusion to contact the lips of the user to tell the user that the DPI is in the correct position. An optional storage section, with a cover, holds additional capsules. The cover for the mouthpiece, and the cover for the storage section may both be transparent magnifying lenses.

The capsules may be two-part capsules where each portion has apertures which correspond to apertures in the other half when each half is partially fitted to the other half, and fully fitted to the other half. All the apertures may be closed when the two halves are rotated around their longitudinal axes with respect to each other. Each capsule may have a unique key on each half that only fits with a particular inhaler.

Therefore it is an object of the invention to provide a dry particle inhaler that can fold into a compact form.

Therefore it is an object of the invention to provide a dry particle inhaler that can be loaded with medicament easily.

Therefore it is an object of the invention to provide a dry particle inhaler where the small writing on a capsule of medicament can be easily read.

Therefore it is an object of the invention to provide a dry particle inhaler where a capsule containing medicament can only be inserted when a person unfolds the inhaler for use.

Therefore it is an object of the invention to provide a dry particle inhaler where the air flow through the device is regulated.

Therefore it is an object of the invention to provide a dry particle inhaler to provide a means for indicating to the user when the air flow is at the correct rate.

Therefore it is an object of the invention to provide a dry particle inhaler where particles of drug are dispersed finely.

These and other objects of the invention will be readily apparent upon a reading of the present specification, claims and drawings.

### **BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS**

Figure 1 is a schematic view of the dry particle inhaler described herein.

Figure 2 is schematic view of the mouthpiece cover.

Figure 3 is schematic view showing the angle between the intake section and the mouthpiece.

Figure 4 is a schematic view of the dry particle inhaler, showing the storage section.

Figure 5 is a schematic view of the intake section of the dry particle inhaler, showing the flow regulator and the feedback module.

Figure 6 is a schematic view of the mixing section.

Figure 7 is a schematic view of a capsule to hold medicament.

Figure 8 is a schematic view of the mouthpiece.

Figure 9 is a perspective view of a specific embodiment of the dry particle inhaler in the closed position, with a capsule inserted into the mixing section, and extra capsules stored in the storage section.

Figure 10 is a perspective view of a specific embodiment of the dry particle inhaler showing a capsule being loaded in to the mixing section.

Figure 11 is a perspective view of a specific embodiment of the dry particle inhaler showing a capsule inserted into the mixing section, and the mouthpiece extended for use.

Figures 12, 13, 14, and 15 follow each other in temporal sequence.

Figure 12 is a perspective view of a specific embodiment of the dry particle inhaler showing a closed mouthpiece cover.

Figure 13 is a perspective view of a specific embodiment of the dry particle inhaler showing an open mouthpiece cover.

Figure 14 is a perspective view of a specific embodiment of the dry particle inhaler showing an open mouthpiece cover, an open mixing section cover, and a capsule about to be inserted into the mixing section.

Figure 15 is a perspective view of a specific embodiment of the dry particle inhaler showing the mouthpiece extended for use.

Figure 16 is a view of a pneumatic circuit, where air flows (fluid flows) are represented by their electrical equivalents.

Figure 17 is a schematic view of the dry particle inhaler.

Figure 18 is a cutaway view of a capsule and a portion of the mixing section.

Figure 19 is a cutaway view of half of a capsule, showing a cone in the interior and a secondary hole with a chamfered, or beveled, edge.

#### **TABLE OF REFERENCE NUMBERS**

10	dry powder inhaler device
20	intake section
30	mixing section
40	mouthpiece
50	air passage through dry powder inhaler device
60	longitudinal axis of intake section
70	longitudinal axis of mouthpiece section
80	swivel joint connecting mouthpiece and mixing section
90	cover for mouthpiece
100	protrusions on mouthpiece cover
110	depressions on dry particle inhaler cover to mate with protrusions on mouthpiece cover
120	tongue depressor on mouthpiece
130	protrusion on surface of mouthpiece to contact lips of device user
135	opening of mouthpiece to be fitted into user's mouth
140	intake port
150	flow regulator

- 160 bleed orifice
- 170 piston
- 180 piston head
- 190 piston rod
- 200 proximal portion of piston rod
- 210 distal portion of piston rod
- 220 spring
- 230 inner walls of intake section inner chamber
- 240 feedback module
- 250 mechanical fasteners in storage section
- 260 holder in mixing section for capsule
- 270 Venturi chamber
- 280 spiral shape or protrusions to impart cyclonic flow to air
- 290 cover for mixing chamber
- 291 interior of mixing section
- 292 air flow entrance to mixing section
- 294 air flow exit from mixing section
- 296 latch mechanism for mixing section cover
- 298 interior wall of mixing section
- 300 capsule
- 310 first tube
- 320 open end of first tube
- 330 closed end of first tube
- 340 long axis of first tube
- 350 protrusion on first tube
- 360 keying surface on first tube
- 370 secondary holes in first tube
- 372 chamfered edge of secondary hole
- 375 cone in interior of first tube
- 380 second tube
- 390 open end of second tube
- 400 closed end of second tube

- 410 long axis of second tube
- 420 protrusion on second tube
- 430 keying surface on second tube
- 440 secondary holes in second tube
- 445 cone in interior of second tube
- 450 hand of user
- 460 air flow direction
- 470 storage section
- 480 storage section cover

### DETAILED DESCRIPTION OF THE INVENTION

Figure 1 is a schematic drawing of the dry powder inhaler (10) described herein. It comprises an intake section (20), a mixing section (30) and a mouthpiece (40). An air passage (50) goes through the intake section (20), a mixing section (30) and a mouthpiece (40). A swivel joint (80) connects the mouthpiece (40) to the mixing section (30). The mixing section (20) has a cover (290) which may be a transparent magnifying lens. Arrow (460) shows the direction of air flow through the air passage (50) through the dry powder inhaler (10).

Figure 2 shows the mouthpiece cover (90) in the closed position over the dry particle inhaler (10). Protrusions (100) on the mouthpiece cover (90) mate with grooves or depressions (110) on the dry particle inhaler (10), to join the mouthpiece cover (90) to the dry particle inhaler (10).

Figure 3 is a schematic of the showing the mouthpiece (40) and the intake section (20) as represented by the longitudinal axis of the mouthpiece (70) and the longitudinal axis of the intake section (60). The swivel joint (80) connecting the mouthpiece (40) to the intake section (20) at the mixing section (30) may be regarded as the vertex of the angle. The importance of the angle (here called theta) between these two longitudinal axes will be further explained.

Figure 4 shows the dry particle inhaler (10) with a storage section (470). Indicated as being inside the storage section (470) are

mechanical fasteners (250) which operate to hold medicament capsules (300) (not shown in this Figure) in the storage section. In this embodiment, the storage section (470) is shown as appended to the intake section (20). The storage section has a cover (480) which may be a transparent magnifying lens, to allow the user to easily read writing on medicament capsules stored therein. The storage section cover (480) may swivel outward, or slide open on a track (not shown), or open by a variety of mechanisms known to those of skill in the art.

Figure 5 shows the intake section (20) of the dry particle inhaler (10). The direction of air flow is shown by the arrow (460). Air is admitted through an intake port (140) and one or more bleed orifices (160) [The bleed orifices may also be styled as secondary ambient air intake ports]. The piston (170) normally covers the intake port (140). When the user (not shown) inspires, the piston head (180) is drawn backwards, at a steady rate modulated by the spring (220). The spring (220) is fixed to the piston (170) and the inner wall (230) of the intake section chamber. Thus the rate of air flow is controlled. The air flow is further controlled by the tapering of the piston rod (190), past which the air flows. For further control of the air flow, a second spring (not shown) may also control the rate of movement of the piston (170).

The piston (170) and spring (220) combination allow the user (not shown) to generate a vacuum in his lungs before the intake port (140) opens. Thus, by the time enough vacuum is generated to open the intake port (140), there will be sufficient air flow at a sufficient rate in the dry particle inhaler (10) to draw most of the medicament in the capsule (not shown) out of the inhaler into the proper place in the lungs of the user.

A feedback module (240) generates a signal to the user (not shown), which tells the user whether he is inspiring at the correct rate. The signal may be an audible one, in one embodiment a tone that is at a steady pitch when air flow is at a certain steady rate. In one embodiment of the dry particle inhaler (10), the signal is generated mechanically, such as be a musical reed. In another embodiment of the invention, the signal might be generated

electronically, after electronic measurement of the air flow rate. The feedback module (240) would include a means for increasing or lessening the signal strength, or turning the signal off entirely. If the signal were generated by a reed, the mechanism for turning off the signal might be covering a bleed orifice which might admit the air flow generating the signal. If the signal were generated electronically, a simple push button or dial might turn on and off the signal.

Figure 6 shows a schematic of the mixing section (30) of the present invention. The mixing section has a cover (290), and a holder (260) for a medicament capsule (not shown). The holder (260) is a mechanism which grips and turns the capsule (not shown) to open and close it as the longitudinal axis (70) of the mouthpiece is rotated about the swivel joint (80) relative to the longitudinal axis (60) of the intake section. Such a mechanism may be straightforward: in a simplest embodiment, both the top and bottom halves (not shown) of the capsule could be fixed to their respective holders (260).

The Venturi chamber (270) speeds the flow of air near the capsule (not shown). Air flows in at (292), and out through (294). In one embodiment, air flows both through and around a capsule (not shown) holding a dry powder medicament. The special shape of the Venturi chamber (270), which further includes protrusions or spiral shapes (280), imparts a cyclonic flow to the air passing through the mixing section (30). This helps to de-agglomerate particles of dry powder. The spiral shape of the interior of the mixing section (291) can be two separate spirals, in one embodiment of the invention. Mixing section (30) therefore provides the means whereby air flow is speeded up to suspend dry particles in air and de-agglomerate them, and then slow the air flow somewhat while the particles are still suspended in air. The cover (290) for the mixing section (30) may be a transparent magnifying lens, so that any writing on the capsule (not shown) may be read easily.

In one embodiment of the dry particle inhaler (10), the cover (290) of the mixing section may not be opened unless the longitudinal axis

(70) of the mouthpiece forms a certain angle with the longitudinal axis (60) of the intake section, with the vertex of the angle being the swivel joint (80) connecting the mouthpiece (40) and the mixing section (30). The latch mechanism (296) for the cover (290) of the mixing section can accomplish this, by any of several mechanical means known to those of ordinary skill in the art. In the simplest embodiment, a catchment (not shown) in the cover (290) for the mixing chamber would be engaged by a slip ring (not shown) on the mixing section which was only a certain number of degrees of a circle. When the mouthpiece (40) were rotated enough relative to the intake section (20), the slip ring (not shown) would no longer engage the catchment (not shown). In one embodiment, the user could open the cover (290) when the angle were between approximately ninety and one-hundred and eighty degrees.

Figure 7 shows a medicament capsule (300) for use with an inhaler, be it a dry powder inhaler (10), or a liquid mist inhaler. The capsule (300) has two halves which fit together, here styled a first tube (310) and a second tube (380). Each tube has an open end (320, 390), and a closed end (330, 400). Each tube also has a long axis (340, 410). In addition, each tube has a number of secondary holes (370, 440). The first tube (310) fits inside the second tube (380) snugly. A protrusion (350) on the outer surface of the first tube (310) can slide past a corresponding protrusion (420) on the inner surface of the second tube (380). This locks the first tube (310) to the second tube (380). Therefore the first tube (310) and the second tube (380) have both an unlocked and a locked position. In the unlocked position, at least one secondary hole (370) in the first tube aligns with at least one secondary hole (440) in the second tube. This permits introduction of a medicament (not shown) into the capsule through the aligned secondary holes (370, 440). The first tube (310) may then be locked to the second tube (380). When a user (not shown) is ready to use a capsule (300), he simply places it in the holder (260) in the mixing section (30), and closes the cover (290). When the holder (260) rotates the first tube (310) around its long axis (340) relative to the second tube (380) and its long axis (410) (the axes are now

coincident), that causes at least two secondary holes (370) in the first tube to align with at least two secondary holes (440) in the second tube. Air can now pass in, through, and out of the capsule (300), releasing the medicament contained therein. In one embodiment of the inhaler, the capsule (300) might open when the angle between the longitudinal axis (70) of the mouthpiece section, the vertex of the swivel joint (80), and the longitudinal axis (70) of the mouthpiece section were between one hundred and seventy and one-hundred and eighty degrees. This rotation of the mouthpiece (40) relative to the intake section (20) would cause a corresponding rotation of the first tube (310) about its long axis (340) relative to the second tube (380) and its long axis (410).

In one embodiment of the invention, several protrusions on the surfaces of the first tube or the second tube might provide a variety of locking positions. Similarly, a variety of secondary holes in the first and second tubes might provide a variety of rotational positions aligning or not aligning secondary holes on the first and second tubes.

The capsules described herein permit the introduction of liquid or gel medicament which can be dried in the capsule, creating a powder. This permits the accurate production of very small amounts of powdered medicament in a capsule, since it can be formed from a larger volume of accurately metered liquid or gel medicament. This permits very accurate microdosing. In addition, chemical reactions and drug mixtures may be made directly in the capsules described herein, then the resulting formulation dried.

In one embodiment of the capsule (300), one or more of the secondary holes (370, 440) used to admit air to the capsule is oval-shaped (elliptical). In one embodiment of the invention, the ratio of the long axis of the ellipse to the shorter axis may be between 1:1 and 3:1, and may be 2:1. This ratio may be called a vertical aspect ratio. In one embodiment of the invention, the intersection of the surface defining one or more of the secondary holes (370, 440) and the surface defining the interior of the

capsule (300) meet in a chamfered, or beveled, edge. This chamfered edge creates a vortex when air flows through the secondary holes (370, 440).

Each capsule (300) also has a keying surface (or fastening mechanism) on the closed end (330) of the first tube and the closed end (400) of the second tube comprising the capsule. The keying surface (360) on the first tube may be different from the keying surface (430) on the second tube. That permits easy tactile and visual identification of the orientation of the capsule. It also permits a system where each drug formulation in a capsule (300) corresponds to a dry particle inhaler (10), so users cannot mix up drugs. In one embodiment of the invention, the keying surface (360) of the first tube mates with a keying surface (430) of a different second tube, or the mechanical fasteners (250) of the storage section (470). This permits easy storage of the capsules (300) in the storage section (470).

Figure 18 shows a medicament capsule (300), with a keying surface (360) on the first tube and a keying surface (430) on the second tube. It also shows a cutaway view of the mixing section (30) and the air flow entrance (292) to the mixing section and the air flow exit (294) to the mixing section. A spiral shape (280) is given to the interior walls (298) of the mixing section, to impart a cyclonic flow to air passing through. The air flow entrance (292) and air flow exit (294) in this embodiment are tangential to the imaginary tube we might call the mixing section interior (291). That is to say, if a radius were drawn perpendicular to the long axis of the tube, and a tangent line were drawn to the circle perpendicular to the radius, the air flow would exit the mixing section along that tangent line. The tangential air flow exit (294) increases the velocity of the air flow, and thus helps disperse the medicament particles. As can be seen from Figure 18, the mixing section interior (291) is sized to accommodate a medicament capsule (300). Keying mechanisms (360, 430) are shaped to mate with holder (260) in the mixing section. Capsules according to the present invention may have a number of shapes, including ovoid and rectangular shapes. A variety of shapes of protrusions and slots may also be employed as keying surfaces. For instance, a keying surface might be a rectangular block, and a capsule holder might

have a rectangular orifice. Alternatively, a keying surface might be triangular, hexagonal, Z-shaped, C-shaped, etc., and the holder would have the correspondingly shaped aperture.

Figure 18 also shows one embodiment of the capsule (300) where a cone (375) is located in the interior of the first tube, and a cone (445) is located in the interior of the second tube. These cones (375, 445) cause the air flow within the capsule to be cyclonic, aiding in mixing the medicament particles with the air. A cone is shown herein, but other cyclone-creating structures are contemplated by the present invention.

Figure 8 shows the mouthpiece (40) of the dry particle inhaler (10). It has a protrusion (130) on its surface to contact the lips of a user (not shown). This helps the user place the mouthpiece correctly in his mouth. The mouthpiece (40) also includes a tongue depressor (120), which may have a bulbous shape. The mouthpiece (40) is long enough that it fits approximately midway into the user's mouth (not shown). This permits greater delivery of medicament to the lungs, and less delivery to the oral cavity. The mouthpiece (40) has a particular aspect ratio of its inner channel (50) (see Figure 17). This slows the air passing through the channel so that the air borne particulates do not end up striking the back of the user's throat. However, the air is not slowed so much that the particulates settle out of the air flow.

Figure 9, Figure 10, and Figure 11 show one specific embodiment of the dry particle inhaler (10). In Figure 9, the cover (90) of the mouthpiece is closed, and several capsule (300) are in the storage section (470). In Figure 10, the mouthpiece (40) has been rotated relative to the intake section (20). The longitudinal axis (60) [not shown] of the intake section here makes an approximately ninety degree angle with the longitudinal axis (70) of the mouthpiece section. This permits the cover (290) for the mixing section to be opened. A medicament capsule (300) taken from the storage section (470) is about to be inserted into the mixing section (30). In Figure 11, the mouthpiece (40) has been rotated to a fully extended position, the cover (290) for the mixing section has been closed,

and the dry particle inhaler 910) is ready for use. In one embodiment of the dry particle inhaler (10), when the dry particle inhaler is in the closed position (Figure 9), the interior of the intake section (20) would be isolated from the outside air, but the mouthpiece (40) interior and the mixing section interior (291) would not be, permitting them to dry out after being exposed to the humid breath of a user.

Figure 12, Figure 13, Figure 14, and Figure 15 show a temporal sequence where a capsule (300) of medicament is loaded into the mixing section (30) of a dry particle inhaler (10), and the mouthpiece (40) is extended for use. The dry particle inhaler (10) described herein can also be used for nasal delivery of medicaments. A small tube (not shown) can be fitted to the end of the mouthpiece (40), and the other end of the tube inserted into the nostril. Alternatively, the mouthpiece (40) may be replaced by a nosepiece (not shown), whose free end is sized to be inserted into a nostril of a user. In another embodiment, a device such as a bellows or a syringe is used to force air through the dry particle inhaler (10) into a nosepiece inserted into the nostril of a user (not shown).

Figure 16 shows the fluid (air) flow of the dry particle inhaler (10) modeled as the equivalent electrical circuit. This is styled a "pneumatic resistance circuit".

Figure 17 shows a schematic view of the dry particle inhaler (10). The air passage (50) through the dry particle inhaler widens as it goes through the mouthpiece (40) along the direction of the air flow (460). The opening (135) of the mouthpiece to be inserted into the mouth of the user may be roughly ellipsoid, or oval, and thus have a major axis and a minor axis. The ratio of these two may be called the horizontal aspect ratio. In one embodiment of the invention, the horizontal aspect ratio is between 2:1 and 4:1. In one embodiment of the dry particle inhaler (10), the horizontal aspect ratio is 3:1. Shaping the opening (135) in this manner keeps the drug particles collimated, maintains the optimal velocity of the particles in the air stream, and is oriented to the natural horizontal aspect ratio of the

oropharyngeal region of the mouth. In one embodiment of the invention, the outline of the opening (135) resembles a bean.

The dry particle inhaler described herein may be used with medicament particles of low, medium, and high shear forces.

The dry particle inhaler and capsules described herein may be made with a variety of suitable materials known to those skilled in the art, such as metal, glass, rubber, and plastic.

While the invention has been described with reference to particular embodiments, those skilled in the art will be able to make various modifications without departing from the spirit and scope thereof.

We claim:

1. A dry powder inhaler comprising:
  - (a) a intake section; mechanically connected to
  - (b) a mixing section; mechanically connected to
  - (c) a mouthpiece;

wherein the intake section, and mouthpiece each have a longitudinal axis;  
and

wherein air flows through a passage extending from the intake section through the mixing section through the mouthpiece; and wherein the mechanical connection between the mouthpiece and the mixing section comprises a swivel joint which allows the longitudinal axis of the intake section to be parallel to the longitudinal axis of the mouthpiece.

2. The dry powder inhaler of claim 1 further comprising a cover mechanically connected to the dry powder inhaler, wherein the cover shelters the mouthpiece.

3. The dry powder inhaler of claim 1 further comprising a cover mechanically connected to the dry powder inhaler, wherein the cover shelters the mixing section.

4. The dry powder inhaler of claim 4 wherein the mixing section cover only opens when the angle defined by the longitudinal axis of the intake section and the longitudinal axis of the mouthpiece and the swivel joint vertex is a fixed number of degrees.

5. The dry powder inhaler of claim 1, wherein the fixed number of degrees the angle must be for the cover to be opened is between approximately ninety degrees and one hundred and eighty degrees.

6. The dry powder inhaler of claim 3 wherein the mixing section cover is translucent and is a magnifying lens.

7. The dry powder inhaler of claim 1 further comprising a storage section mechanically connected to the dry powder inhaler, wherein a cover mechanically connected to the storage section shelters the storage section, and the cover may assume one or more fixed open positions.

8. The dry powder inhaler of claim 7 wherein the storage section cover is translucent and is a magnifying lens.

9. The dry powder inhaler of claim 7 wherein the storage section further includes mechanical fasteners mechanically connected to the storage section to secure capsules within the storage section.

10. The dry powder inhaler of claim 2 wherein the mouthpiece cover is mechanically connected to the dry powder inhaler by means of protrusions on the mouthpiece cover, and wherein the dry powder inhaler further includes corresponding depressions that mate with said protrusions.

11. The dry powder inhaler of claim 1 wherein the intake section includes an inner channel and comprises:

- (a) an intake port; covered by
- (b) a flow regulator; and
- (c) a bleed orifice;

wherein the intake port and the bleed orifice both admit air to the dry powder inhaler, the rate of admission of said air being controlled by both the flow regulator and the bleed orifice and wherein the flow regulator comprises:

(alpha) a piston comprising a piston head connected to a piston rod; and

(beta) one or more springs connected to the piston and the inner walls of the intake chamber; wherein the piston rod wider at the proximal portion connected to the piston head and narrower at the distal portion; and

wherein the piston head covers the intake port; and wherein the piston head moves away from the intake port to admit air to the intake port, and wherein movement of the piston head is modulated by the springs connecting the piston to the inner walls of the intake chamber.

12. The dry powder inhaler of claim 11 wherein the intake chamber further includes a feedback module mechanically connected to the intake chamber, wherein the feedback module generates a signal in response to the flow of air in the intake chamber.

13. The dry powder inhaler of claim 12, wherein the feedback module comprises signal generators selected from the group consisting of electronic apparatuses to generate audio signals and mechanical devices to generate audio signals.

14. The dry powder inhaler of claim 12 wherein the strength of the signal from the feedback module may be varied by a user of the dry powder inhaler.

15. The dry powder inhaler of claim 1, wherein the mixing section is a chamber which comprises a holder for a capsule having top and bottom keying portions; and the holder is nested inside the chamber; wherein the holder mechanically grips the top and bottom keying portions of the capsule, and wherein the holder opens the capsule when the angle defined by the longitudinal axis of the intake section and the longitudinal axis of the mouthpiece and the swivel joint vertex is a fixed number of degrees, and closes the capsule when the angle defined by the longitudinal axis of the intake section and the longitudinal axis of the mouthpiece and the swivel joint vertex is a fixed number of degrees.

16. The dry powder inhaler of claim 1, wherein the fixed number of degrees needed to open the capsule is between approximately ninety degrees and one hundred and eighty degrees, and the fixed number of degrees to close the capsule is between approximately ninety and zero degrees.

17. The dry powder inhaler of claim 1, wherein the mixing section is a chamber which comprises a holder for a capsule having top and bottom keying portions; and the holder is nested inside the chamber; wherein the holder mechanically grips the top and bottom keying portions of the capsule, and the holder only admits one capsule with one type of keying portion.

18. The dry powder inhaler of claim 1, wherein the mixing chamber comprises a Venturi chamber that is shaped to give air passing through it a cyclonic flow.

19. The dry powder inhaler of claim 1, wherein the Venturi chamber is shaped so as to keep the air velocity below the inflection speed limit.
20. A dry powder inhaler comprising a mouthpiece sized to extend mid-way into the oral cavity of a user.
21. The dry powder inhaler of claim 20 wherein the mouthpiece further includes a tongue depressor.
22. The dry powder inhaler of claim 21 wherein the tongue depressor has a bulbous shape.
23. The dry powder inhaler of claim 1 wherein the mouthpiece has an outer surface further includes a protrusion on that outer surface to contact the lips of the user and so to indicate to the user that the dry powder inhaler has been inserted into the oral cavity of the user in the correct position.
24. The dry powder inhaler of claim 1 wherein the mouthpiece has an inner channel shaped to keep air flowing at the proper velocity of approach.
25. The dry powder inhaler of claim 2 wherein air is admitted to dry the mouthpiece when the cover is closed.
26. The dry powder inhaler of claim 1 wherein the mouthpiece opening has an approximately 3:1 horizontal aspect ratio.
27. The dry powder inhaler of claim 1 wherein the inhaler was designed using a pneumatic resistance circuit.
28. A capsule for holding a medicament comprising a first tube and a second tube, wherein:
  - (a) a first tube having a long axis, having an inner and an outer surface radial to the long axis, wherein the tube is open at one end perpendicular to the long axis and closed at one end perpendicular to the long axis; and wherein the first tube has at least one protrusion on its outer surface; and
  - (b) a second tube having a long axis, having an inner and an outer surface radial to the long axis, wherein the tube is open at one end

perpendicular to the long axis and closed at one end perpendicular to the long axis and wherein the second tube has at least one protrusion on its inner surface; and wherein the outer circumference of the first tube is approximately equal to the inner circumference of the second tube, such that the open end of the first tube can slide snugly into the open end of the second tube; and wherein a protrusion on the outer surface of the first tube may slide past a protrusion on the inner surface of the second tube, locking the tubes together;

and wherein the first tube and the second tube each have one or more secondary holes other than the openings at the end of each tube, wherein at least one secondary hole in the first tube may be made coincident with at least one secondary hole in the second tube when the first tube is slid onto the second tube in the unlocked position by rotation of the first and second tubes about their long axes, and

wherein when the first tube is locked onto the second tube at least two secondary holes in the first tube may be made coincident with at least two secondary holes in the second tube by rotation of the first and second tubes about their long axes.

29. The capsule of claim 28 wherein the first and second tubes further comprise keying surfaces at the closed ends of the tubes.

30. The capsule of claim 28 further including medicament selected from the group consisting of liquid, powder, and gaseous medicaments.

31. A medicament capsule comprising a fastening mechanism to attach it to a second medicament capsule.

32. The medicament capsule of claim 31 wherein the fastening mechanism can attach the capsule to a storage compartment for capsules in an inhaler.

33. A medicament capsule for an inhaler wherein the medicament capsule comprises apertures in the capsule to admit air flow and wherein structures in the interior surface of the capsule create cyclonic air flow.

34. The capsule of claim 33 wherein the structures are cone-shaped.

35. A medicament capsule for a dry particle inhaler having a hole to admit air flow to release medicament into the airstream of the dry particle inhaler wherein the vertical slot ratio of the hole is between 1:1 and 3:1.

36. The medicament capsule of claim 35, wherein the vertical slot ratio is 2:1.

37. A method of making a capsule comprising a powdered medicament comprising the steps of:

(a) introducing a liquid or gel containing medicament into the capsule of claim 28; and

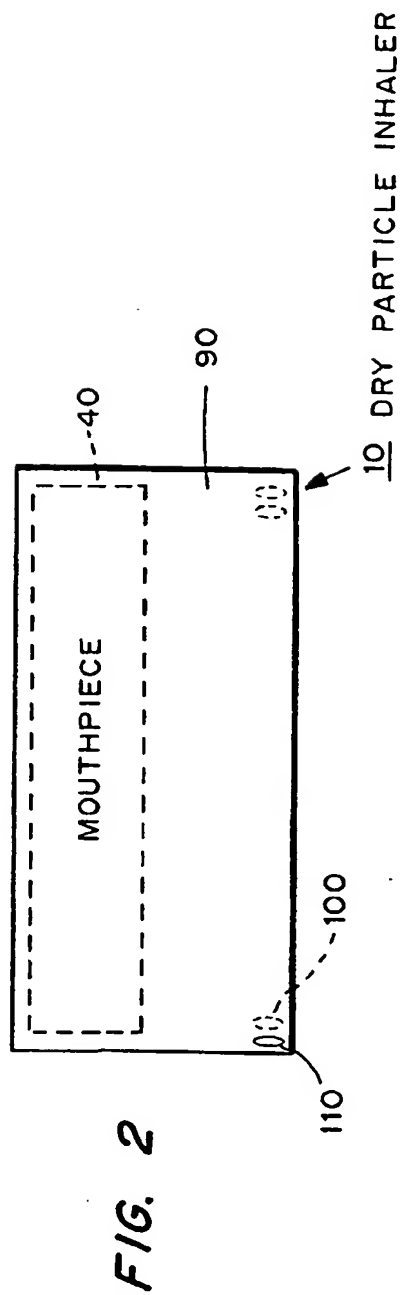
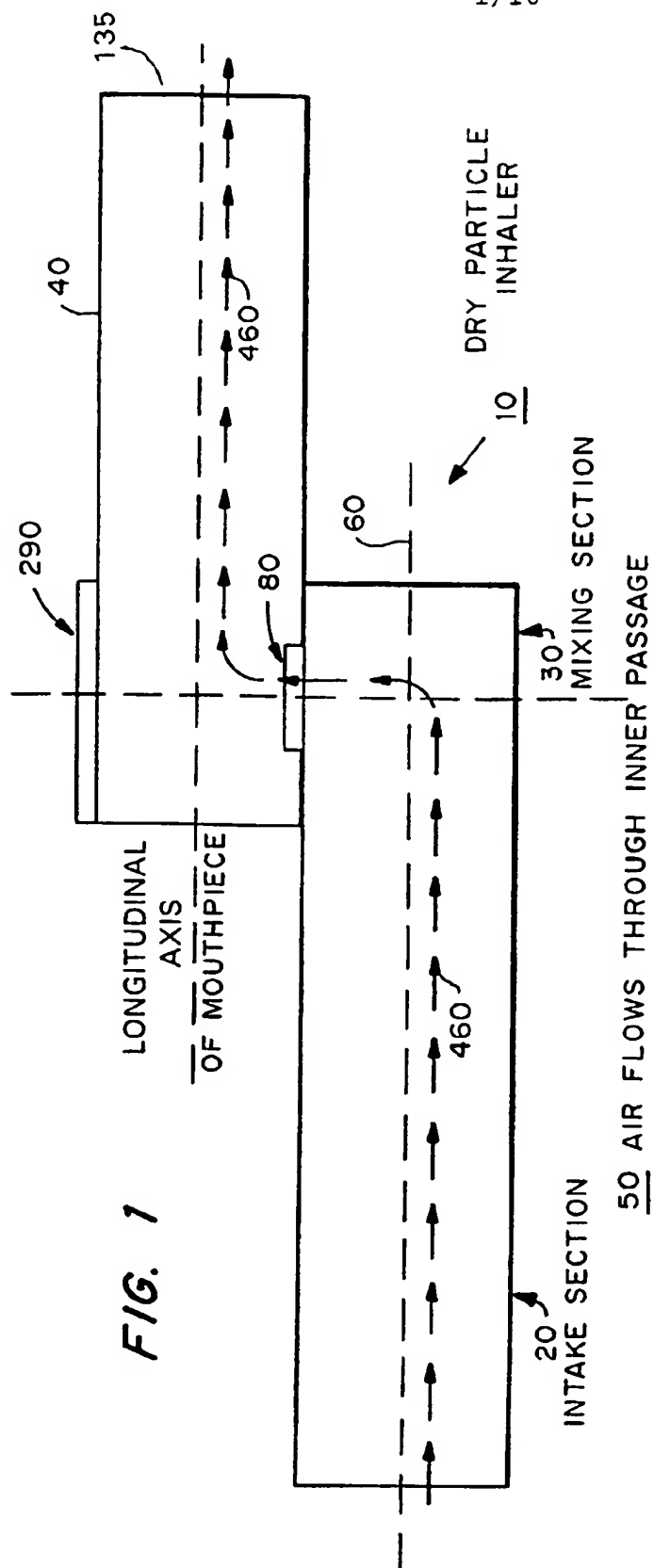
(b) drying the medicament to form a powder.

38. A method of making a capsule comprising a medicament comprising the step of introducing one or more chemicals into the capsule of claim 28.

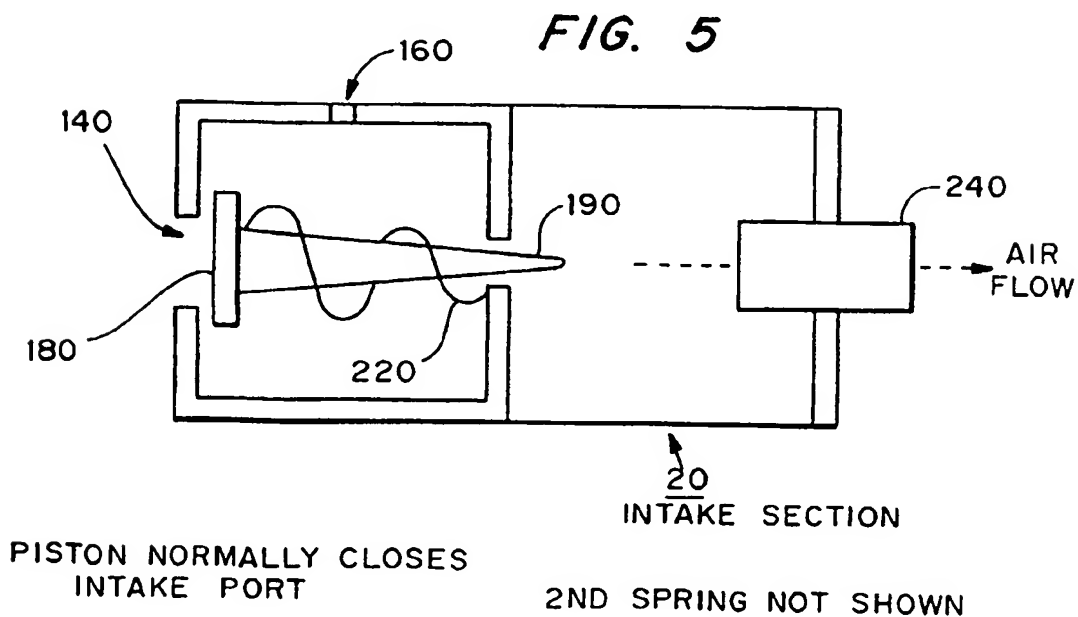
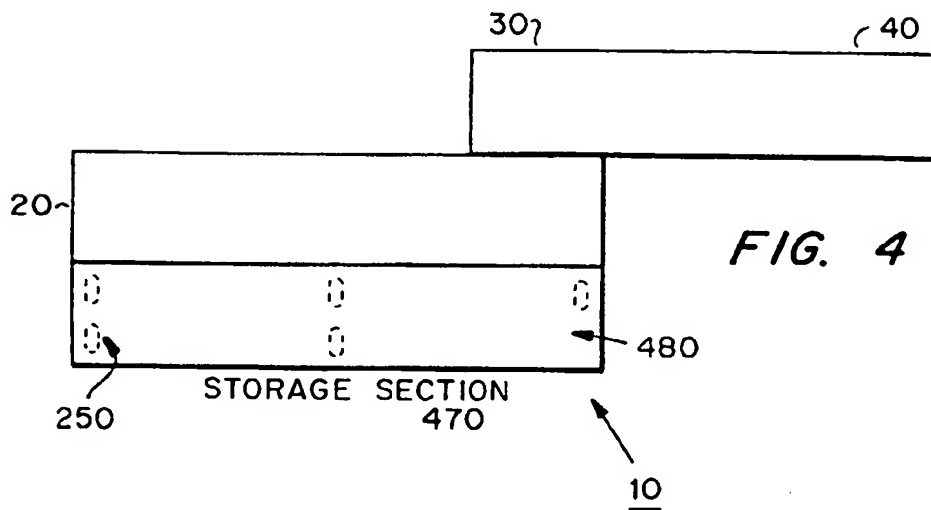
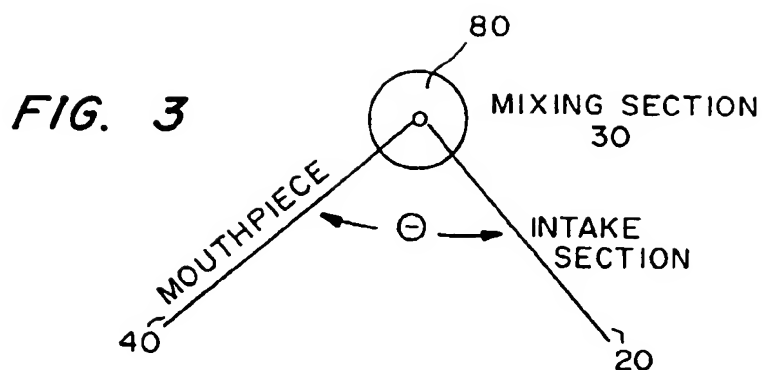
39. The dry particle inhaler of claim 1, wherein the inner channel of the intake section may be isolated from outside air while the inner channel of the mixing section and the mouthpiece is exposed to outside air.

40. The dry particle inhaler of claim 1, wherein the mixing section has a long axis, and wherein the air flowing through the mixing section to the mouthpiece exits the mixing section at a tangent to a circle described by a radius about the long axis of the mixing section.

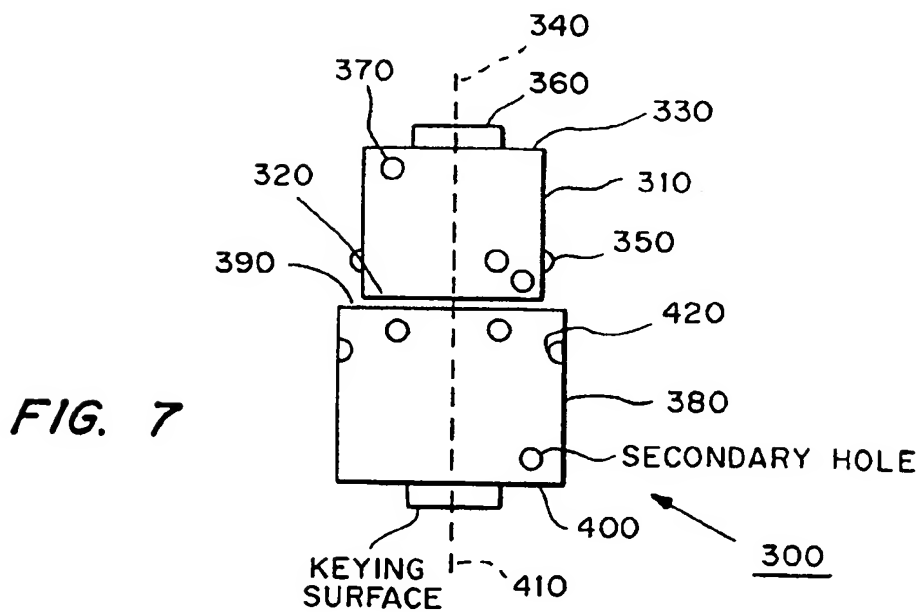
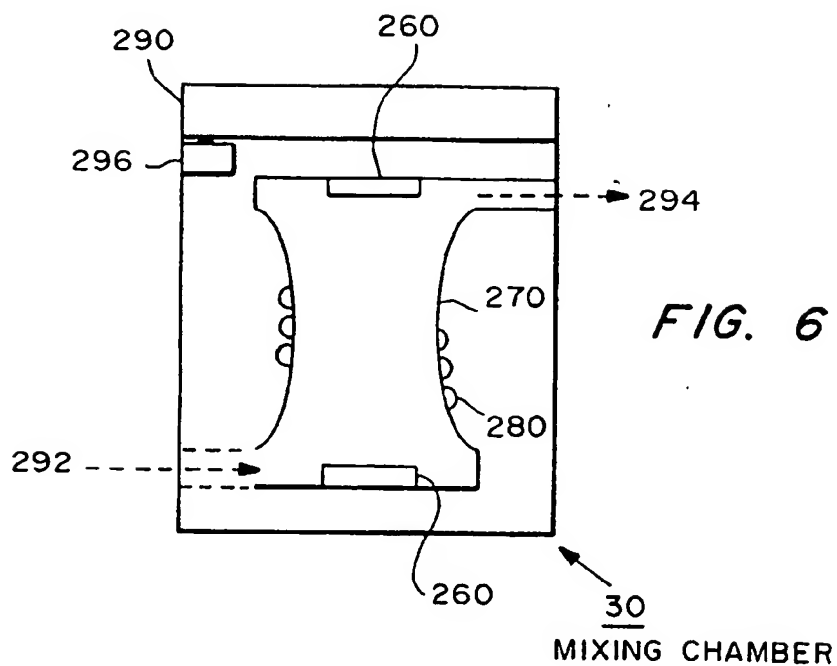
1/10



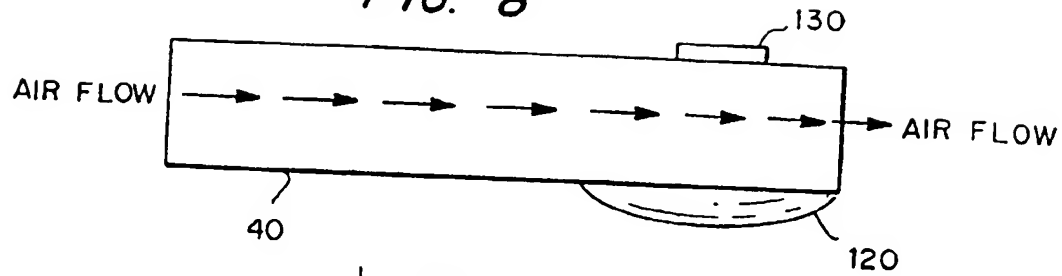
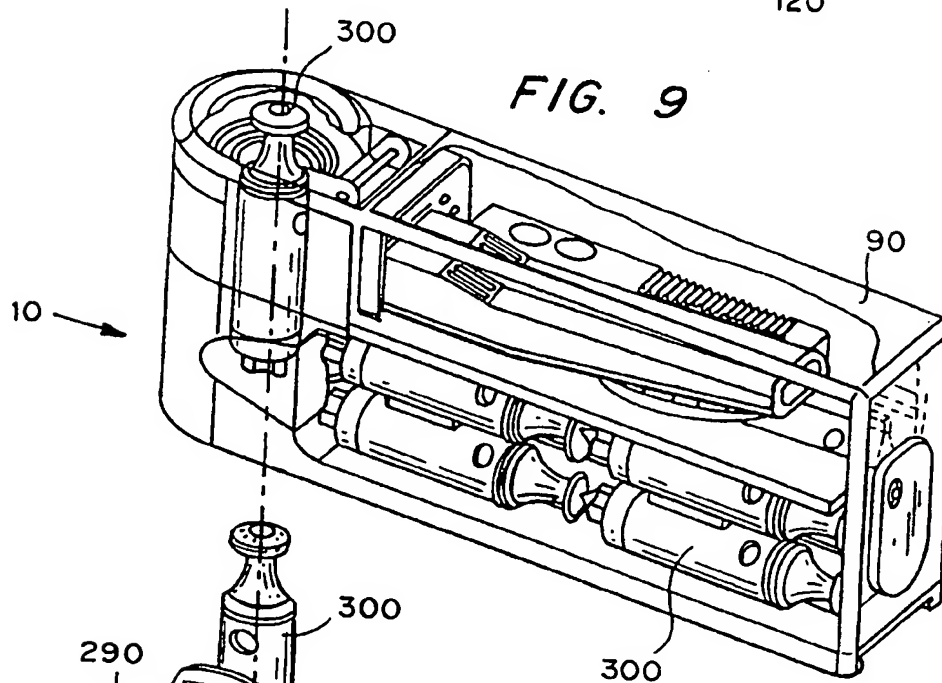
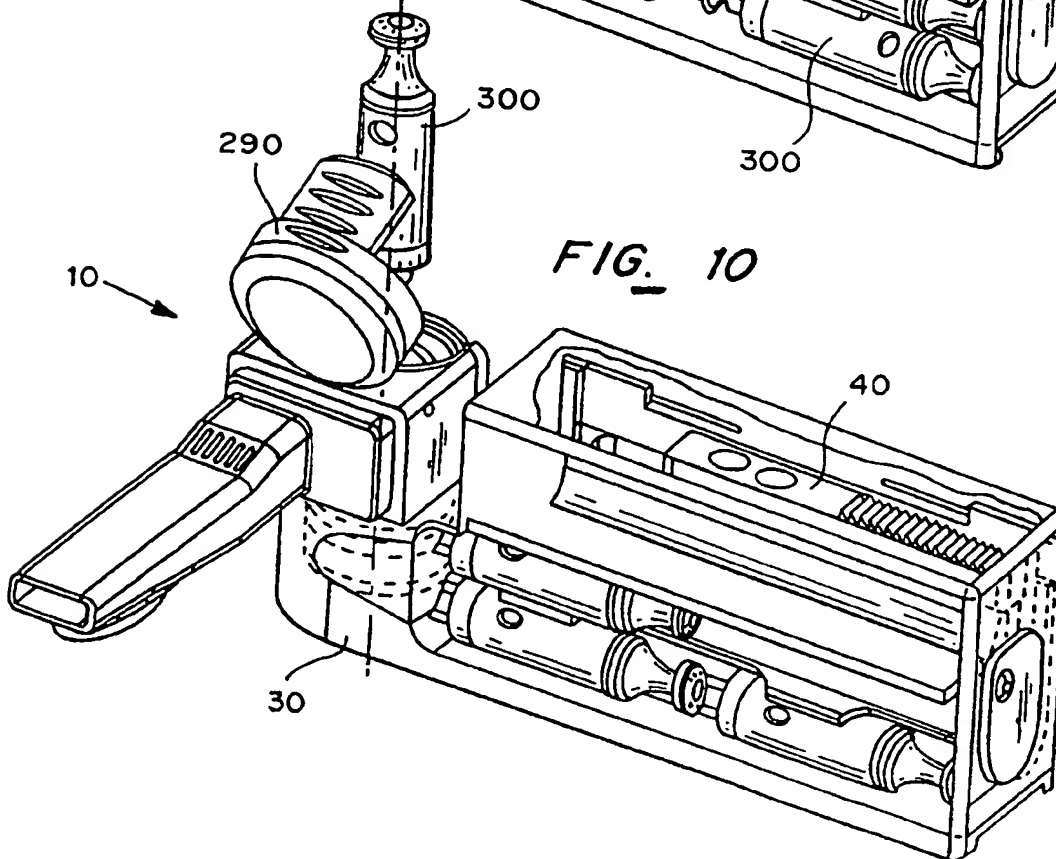
2/10



3/10

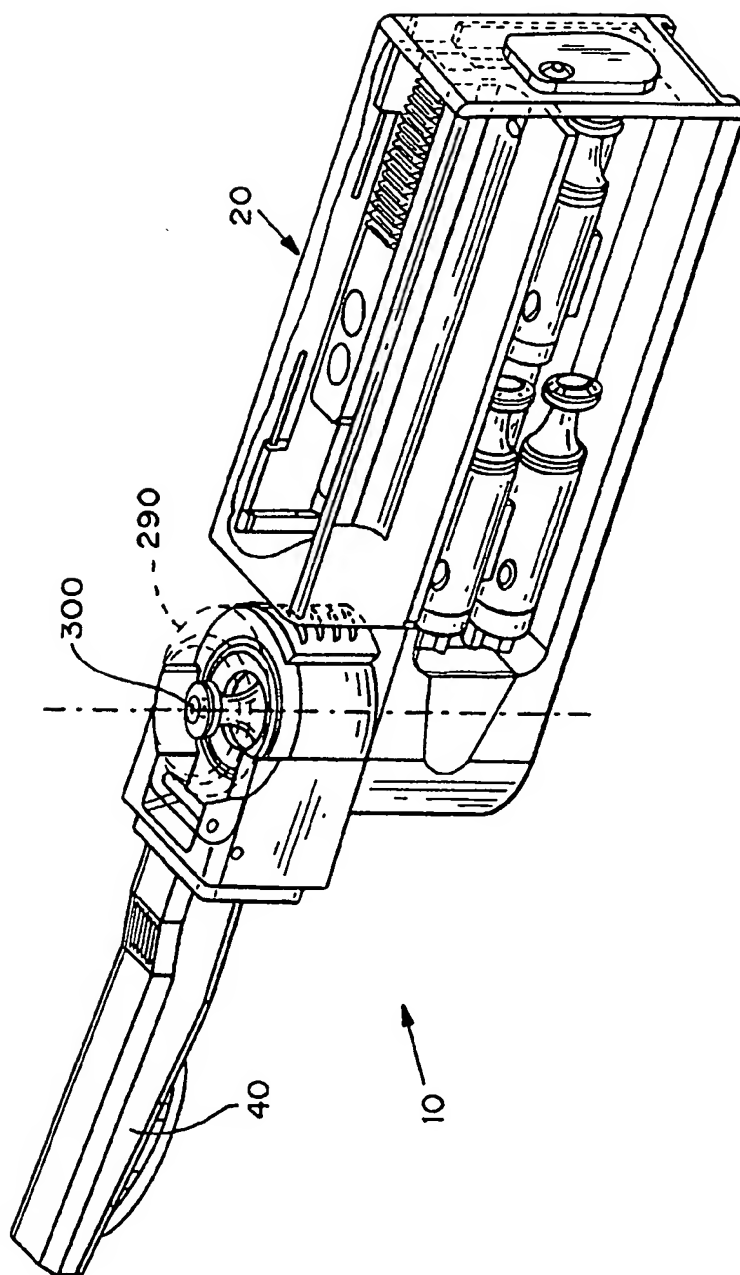


4/10

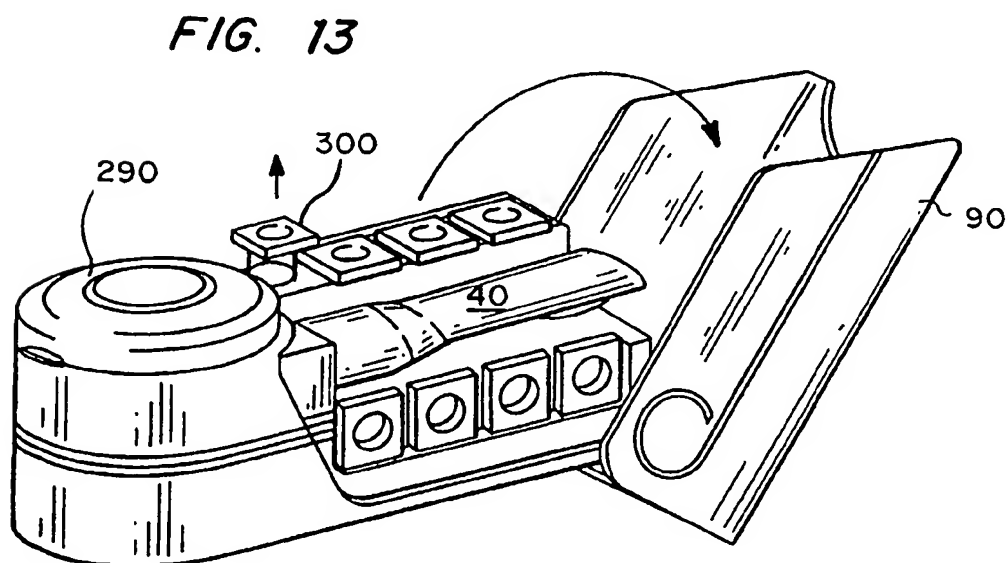
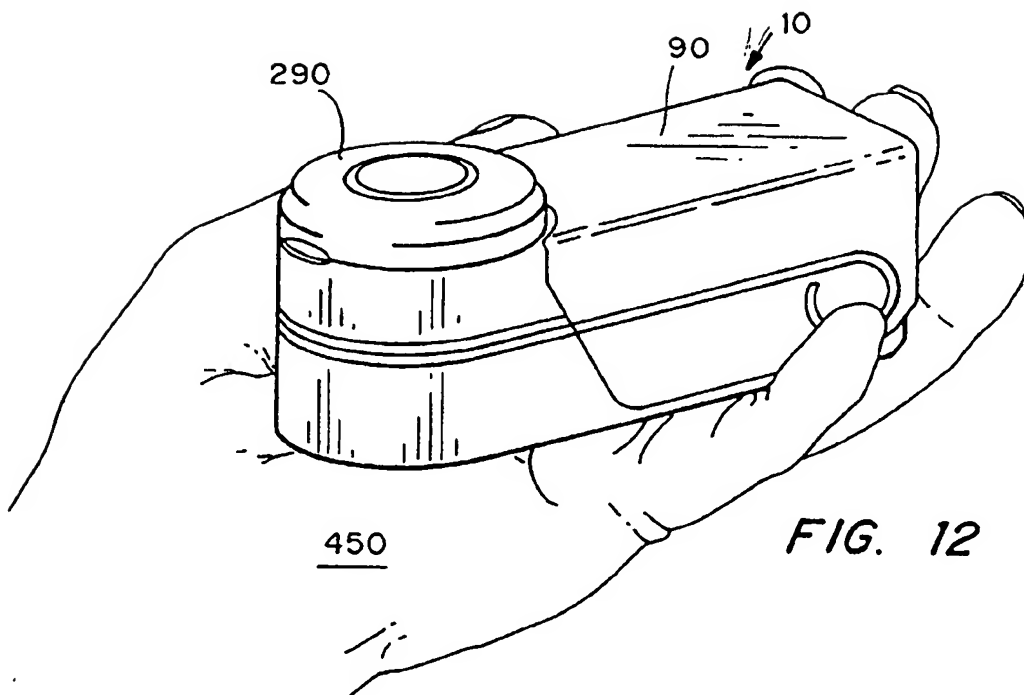
**FIG. 8****FIG. 9****FIG. 10**

5/10

FIG. 11

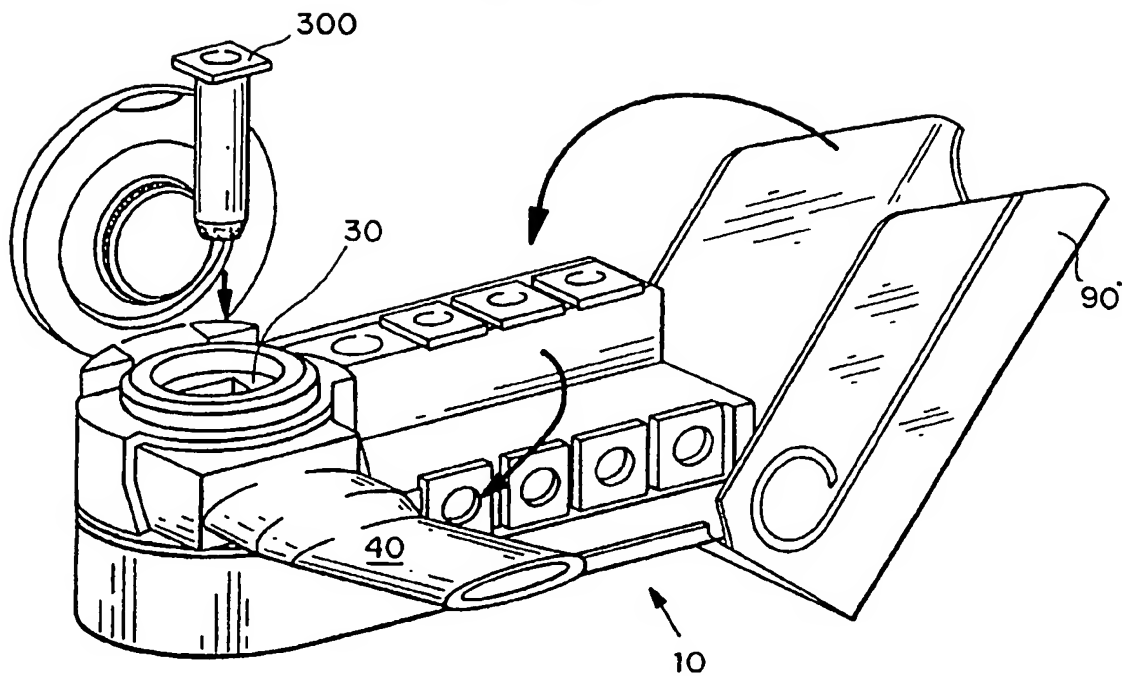


6/10



7/10

**FIG. 14**



**FIG. 15**

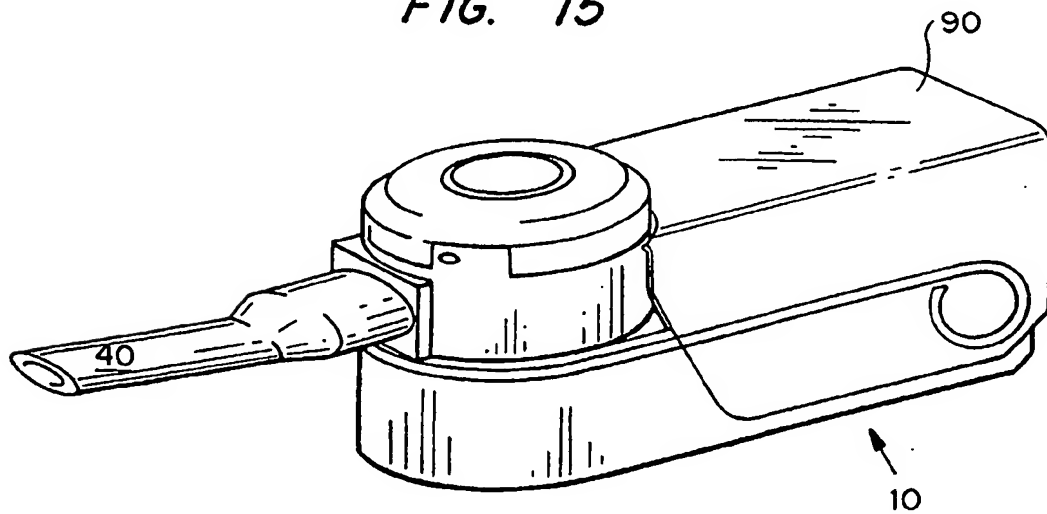


FIG. 16

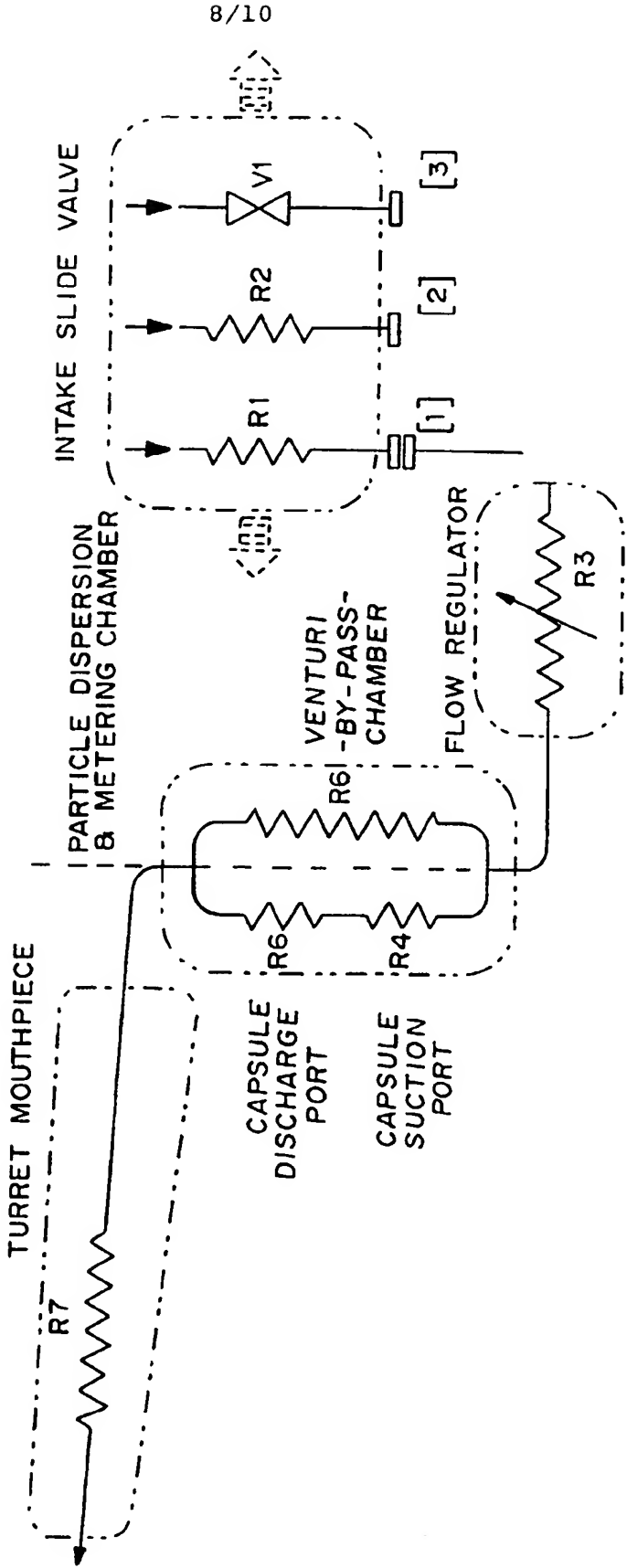
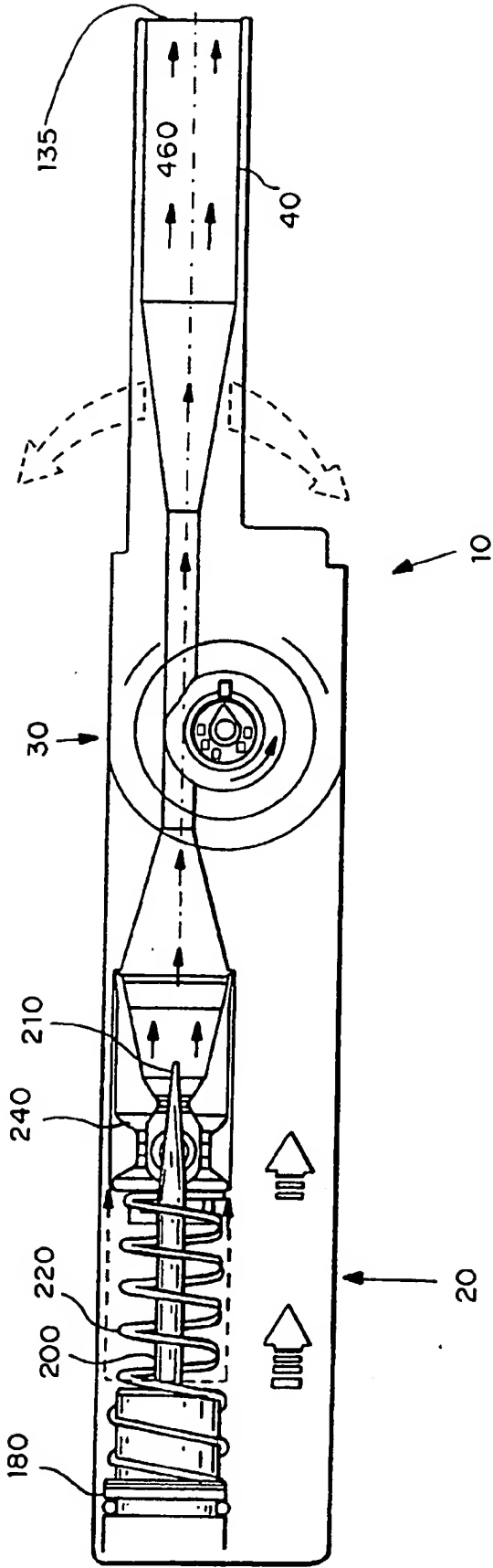
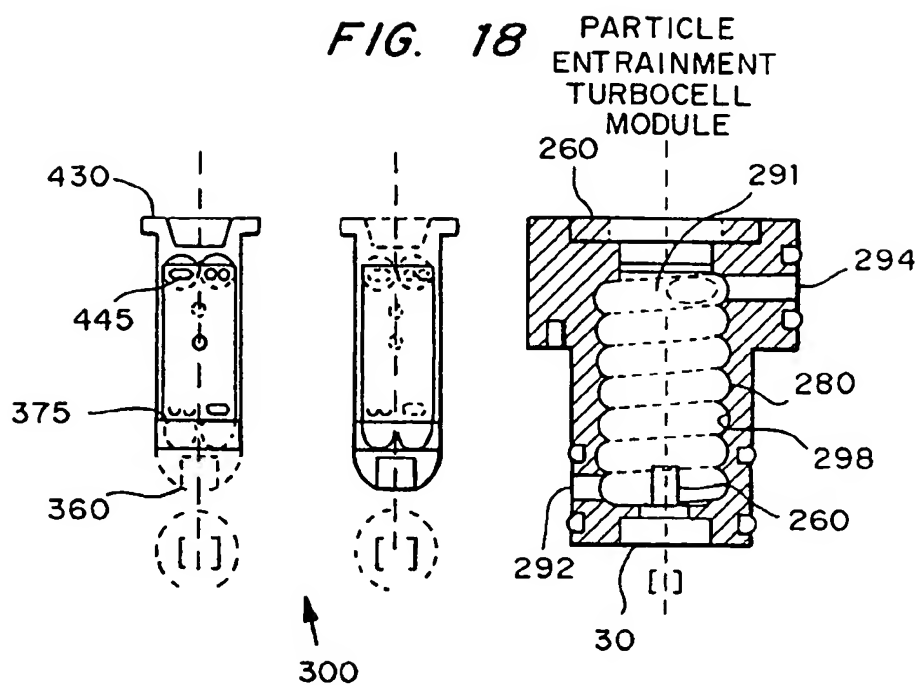
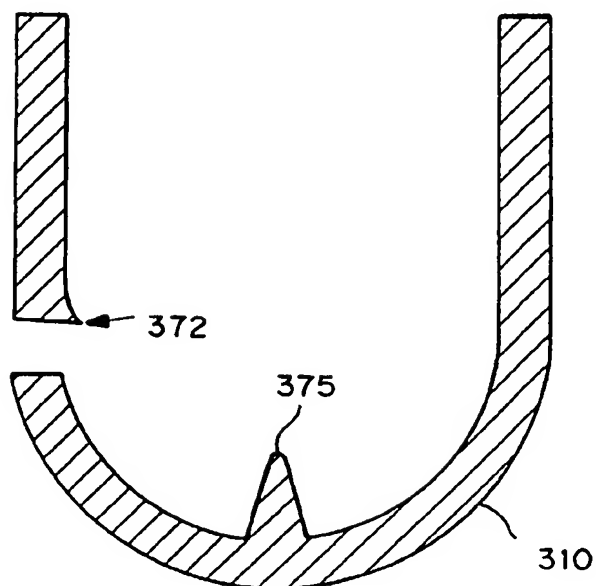


FIG. 17



10/10

**FIG. 19**

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/40454

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 A61M15/00 A61J3/07

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61M A61B A61F A61K A61L A61N A61J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 072 536 A (MALEM H) 7 October 1981 (1981-10-07) the whole document	1,20,23
A	WO 96 22802 A (DIRECT HALER A S ;KELDMANN ERIK (DK); REIPUR JOHN (DK)) 1 August 1996 (1996-08-01) abstract; figure 1	1,2
A	page 12, line 18 -page 13, line 6; figures 5,6	20,23
A	DE 36 39 836 A (BECHTER SIGRID) 1 June 1988 (1988-06-01) the whole document	1,2
	--- -/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

21 February 2001

Date of mailing of the international search report

12. MRZ. 2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 cpo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Jameson, P

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/40454

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 41255 A (JENNINGS DOUGLAS ; ASTRA AB (SE); JEPPSSON MAGNUS (SE)) 24 September 1998 (1998-09-24) page 9, line 10 - line 22 ---	6,8
A	US 5 524 613 A (SMEDLEY WILLIAM H ET AL) 11 June 1996 (1996-06-11) column 2, line 15 - line 31 ---	6,8
A	US 5 758 638 A (KREAMER JEFFRY W) 2 June 1998 (1998-06-02) abstract ---	12,13
A	EP 0 581 473 A (BESPAK PLC) 2 February 1994 (1994-02-02) abstract; figure 11 ---	15,17
A	US 5 797 391 A (COOK ROBERT STANLEY ET AL) 25 August 1998 (1998-08-25) abstract ---	15
A	column 6, line 27 - column 7, line 18; figure 5 ---	7
A	US 4 047 525 A (KULESSA GERHARD ET AL) 13 September 1977 (1977-09-13) the whole document ---	1
A	WO 98 26827 A (INNOVATA BIOMED LTD ;BRAITHWAITE PHILIP (GB)) 25 June 1998 (1998-06-25) abstract; figure 1 ---	18
Y	US 4 487 327 A (GRAYSON ROBERT E) 11 December 1984 (1984-12-11) abstract; figures 1-14 ---	28,30,38
Y	US 5 170 801 A (MCCARTNEY MICHAEL L ET AL) 15 December 1992 (1992-12-15) abstract; figure 3 column 3, line 27-53 ---	28,30,38
A	US 3 823 816 A (WHEELER L ET AL) 16 July 1974 (1974-07-16) abstract; figures 1,2 ---	28,30, 37,38
A	US 4 040 536 A (SCHWARZ ERWIN) 9 August 1977 (1977-08-09) abstract; figures 1-6 ---	28
X	GB 2 148 841 A (WARNER LAMBERT CO) 5 June 1985 (1985-06-05) the whole document ---	31
A	the whole document ---	32
	--- -/--	

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/40454

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 308 637 A (STEPHAN DIETER ;STEPHAN GUENTER (DE)) 29 March 1989 (1989-03-29) abstract; figures 1-4 ---	31
X	DE 195 19 840 A (KAEWERT KLAUS ;SUES WALTER (DE)) 5 December 1996 (1996-12-05) abstract; figures 1-5 ---	31
A	US 5 896 855 A (COOK ROBERT S ET AL) 27 April 1999 (1999-04-27) abstract; figure 3 ---	32
A	EP 0 666 085 A (PLURICHEMIE ANSTALT) 9 August 1995 (1995-08-09) the whole document -----	33,35

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/40454

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-27, 39-40

Dry powder inhaler with intake, mixing and mouthpiece sections and a swivel joint between the mouthpiece and mixing sections.

2. Claims: 28-30, 37-38

Medicament capsule with two tube construction and method of manufacture .

3. Claims: 31-32

Medicament capsule with fastening mechanism

4. Claims: 33-34

Medicament capsule with apertures and cyclonic flow producing structures

5. Claims: 35-36

Medicament capsule with hole for air flow having vertical slot ratio specified.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/40454

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 2072536 A	07-10-1981	AT 8337 T	15-07-1984
		AU 544841 B	13-06-1985
		AU 6787381 A	09-10-1981
		DE 3164656 D	16-08-1984
		EP 0048244 A	31-03-1982
		ES 500713 D	16-05-1982
		ES 8204924 A	01-09-1982
		FI 813560 A	10-11-1981
		WO 8102676 A	01-10-1981
		HK 39884 A	11-05-1984
		JP 57500364 T	04-03-1982
		NO 813908 A	18-11-1981
		US 4452239 A	05-06-1984
		ZA 8101942 A	23-02-1983
WO 9622802 A	01-08-1996	AT 190512 T	15-04-2000
		AU 693306 B	25-06-1998
		AU 4385896 A	14-08-1996
		BR 9606838 A	30-11-1999
		CA 2210717 A	01-08-1996
		CN 1169117 A	31-12-1997
		CZ 9702103 A	17-12-1997
		DE 69607143 D	20-04-2000
		DE 69607143 T	16-11-2000
		DK 805696 T	05-06-2000
		EA 52 B	30-04-1998
		EP 0805696 A	12-11-1997
		ES 2145421 T	01-07-2000
		FI 973079 A	22-09-1997
		GR 3033542 T	29-09-2000
		HU 9900352 A	28-05-1999
		JP 10512478 T	02-12-1998
		NO 973371 A	22-07-1997
		NZ 298384 A	28-07-1998
		PL 321495 A	08-12-1997
		PT 805696 T	31-08-2000
		SK 93897 A	04-02-1998
		TR 9700669 T	21-02-1998
DE 3639836 A	01-06-1988	NONE	
WO 9841255 A	24-09-1998	AU 6430298 A	12-10-1998
		EP 1017437 A	12-07-2000
US 5524613 A	11-06-1996	AU 7637694 A	22-03-1995
		WO 9506491 A	09-03-1995
US 5758638 A	02-06-1998	NONE	
EP 0581473 A	02-02-1994	AT 156372 T	15-08-1997
		DE 69312820 D	11-09-1997
		DE 69312820 T	27-11-1997
		US 5379763 A	10-01-1995
US 5797391 A	25-08-1998	AT 168891 T	15-08-1998
		AU 652242 B	18-08-1994
		AU 1550392 A	02-11-1992
		CA 2104290 A	29-09-1992

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/40454

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5797391 A		CZ 9301984 A	16-03-1994
		DE 69226444 D	03-09-1998
		DE 69226444 T	28-01-1999
		EP 0506293 A	30-09-1992
		EP 0613384 A	07-09-1994
		FI 934239 A	27-09-1993
		WO 9217233 A	15-10-1992
		HU 67134 A	28-02-1995
		IE 920952 A	07-10-1992
		IL 101389 A	31-07-1995
		JP 6505897 T	07-07-1994
		MX 9201351 A	01-01-1993
		NO 933436 A	27-09-1993
		NZ 242031 A	27-01-1995
		SK 103693 A	06-04-1994
		ZA 9202026 A	25-11-1992
		AT 145145 T	15-11-1996
		AU 652243 B	18-08-1994
		AU 1564792 A	02-11-1992
		CA 2104291 A	29-09-1992
		CZ 9402904 A	15-03-1995
		DE 69215217 D	19-12-1996
		DE 69215217 T	07-05-1997
		EP 0506292 A	30-09-1992
		EP 0576504 A	05-01-1994
		FI 934238 A	27-09-1993
		WO 9217232 A	15-10-1992
		HU 67203 A	28-02-1995
		IE 920951 A	07-10-1992
		IL 101390 A	31-07-1995
		JP 6505896 T	07-07-1994
		MX 9201350 A	01-01-1993
		NO 933463 A	28-09-1993
		NZ 242030 A	27-01-1995
		ZA 9202027 A	25-11-1992
US 4047525 A	13-09-1977	DE 2502251 A	22-07-1976
		BE 837638 A	16-07-1976
		CH 596841 A	31-03-1978
		FR 2297638 A	13-08-1976
		JP 51097292 A	26-08-1976
		NL 7600241 A	20-07-1976
WO 9826827 A	25-06-1998	AU 7735998 A	15-07-1998
		EP 0959926 A	01-12-1999
US 4487327 A	11-12-1984	NONE	
US 5170801 A	15-12-1992	CA 2052562 A	03-04-1992
		JP 6023020 A	01-02-1994
		WO 9205822 A	16-04-1992
		US 5167626 A	01-12-1992
US 3823816 A	16-07-1974	AR 196325 A	18-12-1973
		AU 463254 B	17-07-1975
		AU 5171973 A	08-08-1974
		BE 794951 A	29-05-1973
		CA 990238 A	01-06-1976

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/40454

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 3823816 A		DE 2305280 A ES 411206 A FR 2170751 A GB 1377452 A IT 977185 B JP 1043060 C JP 48082025 A JP 55032381 B ZA 7300766 A	09-08-1973 01-04-1976 14-09-1973 18-12-1974 10-09-1974 23-04-1981 02-11-1973 25-08-1980 25-09-1974
US 4040536 A	09-08-1977	NONE	
GB 2148841 A	05-06-1985	BE 900950 A CH 661878 A DE 3438656 A FR 2554418 A IT 1178193 B JP 1947556 C JP 6073539 B JP 60132562 A US 4738724 A US 4738817 A	30-04-1985 31-08-1987 23-05-1985 10-05-1985 09-09-1987 10-07-1995 21-09-1994 15-07-1985 19-04-1988 19-04-1988
EP 0308637 A	29-03-1989	DE 3727894 A DK 457288 A FI 883785 A NO 883667 A	02-03-1989 22-02-1989 22-02-1989 22-02-1989
DE 19519840 A	05-12-1996	NONE	
US 5896855 A	27-04-1999	AT 163553 T AU 5710294 A CA 2152168 A DE 69317302 D DE 69317302 T DK 675742 T EP 0675742 A EP 0806214 A ES 2115923 T WO 9414491 A GR 3026661 T JP 8504634 T MX 9400086 A ZA 9309705 A	15-03-1998 19-07-1994 07-07-1994 09-04-1998 20-08-1998 28-09-1998 11-10-1995 12-11-1997 01-07-1998 07-07-1994 31-07-1998 21-05-1996 29-07-1994 29-08-1994
EP 0666085 A	09-08-1995	PT 101450 A AT 190511 T AU 698047 B AU 1140795 A BR 9500536 A CA 2141465 A CN 1111160 A CZ 9500210 A DE 69515536 D DE 69515536 T DK 666085 T ES 2145212 T FI 950444 A	09-08-1995 15-04-2000 22-10-1998 10-08-1995 25-03-1997 03-08-1995 08-11-1995 11-09-1996 20-04-2000 10-08-2000 05-06-2000 01-07-2000 03-08-1995

# INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/US 00/40454

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0666085 A		GR 3032986 T	31-07-2000
		HR 950042 A	30-04-1997
		HU 71287 A, B	28-11-1995
		JP 7222800 A	22-08-1995
		NO 950368 A	03-08-1995
		NZ 270403 A	25-03-1998
		PL 307011 A	07-08-1995
		SI 9500036 A	31-08-1995
		SK 11995 A	09-08-1995
		US 5673686 A	07-10-1997
		ZA 9500356 A	14-12-1995
-----			